Lebrikizumab improves signs and symptoms of moderate-to-severe atopic dermatitis in patients not adequately controlled or non-eligible for cyclosporine: a placebo-controlled, randomized phase 3 clinical study (ADvantage)

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**Introduction:** Lebrikizumab (LEB), a novel monoclonal antibody with high affinity and slow off-rate to interleukin-13, is efficacious and safe in adults and adolescents with moderate-to-severe atopic dermatitis (AD). Efficacy of cyclosporine A (CsA), used for severe AD, may not be optimal in some AD patients and its safety limits long-term use.

**Objectives:** We report 16-week efficacy and safety of LEB + low-/mid-potency topical corticosteroids (TCS) in patients with moderate-to-severe AD, not adequately controlled/non-eligible for CsA, in the phase 3 ADvantage study.

**Methods:** ADvantage had a 16-week, randomized, double-blind, PBO-controlled, parallel-group period followed by a 36-week open-label maintenance period. Eligibility: adults and adolescents (age ≥12 - <18 years), Eczema Area and Severity Index (EASI) ≥16, Investigator’s Global Assessment (IGA) ≥3, ≥10% body surface area of AD involvement, and patients not adequately controlled or non-eligible for CsA. Randomization: 2:1 to LEB 250 mg with a loading dose of LEB 500 mg at baseline and week-2, or PBO every two weeks (Q2W). All patients received concomitant mid-potency TCS through week-16; dosage
tapered once lesions were controlled and stopped after 7 days. Primary endpoint: percentage of patients achieving 75% reduction in EASI (EASI 75) at week-16. Secondary endpoints: percentage of patients achieving EASI 90, IGA 0/1, and ≥4-point improvement in pruritus Numeric Rating Scale (NRS) at week-16. Safety endpoints: treatment-emergent adverse events (TEAEs), serious adverse events (SAEs) and TEAEs causing discontinuation.

**Results:** 312/331 patients (212 LEB+TCS and 100 PBO+TCS) completed the 16-week period. At week 16, significantly higher proportion of LEB+TCS vs PBO+TCS patients achieved EASI 75 (68.4% vs 40.8%, p<0.001) and EASI 90 (42.9% vs 20.8%, nominal p<0.001); higher percentage of patients achieved IGA 0/1 (42.0% vs 24.5%, nominal p<0.01) and ≥4-point improvement in pruritus NRS (49.9% vs 29.7%, nominal p<0.05). TEAEs: 61.8% LEB+TCS vs 53.2% PBO+TCS, with nasopharyngitis and conjunctivitis being the most common TEAEs. SAEs and TEAEs causing discontinuation were low and similar in both groups.

**Conclusions:** At week 16, LEB 250 mg Q2W + TCS significantly improved AD signs and symptoms in adults and adolescents with moderate-to-severe AD and history of inadequate response to CsA, or for whom CsA was not advisable.

**Keywords:** Lebrikizumab, Topical corticosteroids, Investigator Global Assessment, Eczema Area and Severity Index, Pruritis Numeric Rating Scale.

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